
Ménière's Disease and Tinnitus

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Abstract

Tinnitus is one of the Ménière's disease clue symptoms, but by far less studied than vertigo or other types of dizziness. The typical Ménière's tinnitus is a low pitched fluctuating one. Although controversial, cochlear Ménière's disease may account for a tinnitus subtype, a fact that may impact on tinnitus diagnosis and treatment. Further studies focused on tinnitus are necessary to clarify at which extent Ménière's disease may have a role in some types of chronic tinnitus.

Keywords: tinnitus, Ménière's disease, hearing loss, vertigo, dizziness

1. Introduction

Ménière disease (MD) is a chronic inner ear condition that was first described by Prosper Ménière in the nineteenth century [1]. His initial description of the disease including hearing loss, vertigo and tinnitus was accurate, but the pathophysiology of the condition was only described 75 years later. The endolymphatic hydrops is the main finding, initially ascertained only in post-mortem exams and nowadays detectable in high resolution magnetic resonance imaging (MRI) [2].

The reported prevalence of MD is 190–513/100,000 cases [3]. Classical symptoms include fluctuating hearing loss, aural fullness and periodic vertigo and tinnitus [2]. The diagnosis criteria from the American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS)

and the Bárány Society do not recognize an eventual 'cochlear' Ménière disease [4], but recent imaging studies (gadolinium contrasted 3T MRI) are more sympathetic with this possibility [5].

Although virtually all patients that fulfilled the AAO-HNF clinical criteria for MD whose inner ears were evaluated post-mortem exhibited endolymphatic hydrops (EH), not all the patients with Proven EH developed MD [2]. Many theories concerning the pathophysiology of MD have been proposed, including changes in endolymph reabsorption due to anatomical variations, perfusion/reperfusion vascular changes, autoimmune mechanisms and changes in water homeostasis [6]. Aquaporins (AQP) are involved in fluid regulation in the inner ear, specifically the subtypes AQP 1, 4 and 6 [6, 7]. It has been demonstrated that vasopressin and oxytocin have a direct effect on aquaporin-mediated regulation of inner ear fluids [7]. Moreover, cytochemical changes in AQP 4 and 6 expressions in the cochlear supporting cells were demonstrated in MD inner ears [6].

2. Current trends of thoughts concerning tinnitus pathophysiology

Tinnitus is the perception of noise which is not generated by external stimulus [8]. It affects approximately 25% of the general population; one third on a frequent basis [9]. Tinnitus may be classified as auditory and para-auditory tinnitus, with the former representing the majority of cases and the latter being subdivided into muscular and vascular tinnitus, sometimes referred as somatosounds [10].

According to the most recent trends of thought, tinnitus is not considered a disease, but a symptom, which may have multiple causes, sometimes even in a single patient [11, 12]. Noise exposure, metabolic and cardiovascular disease, presbycusis, ototoxicity and cranial and cervical trauma are the most frequently considered causes of tinnitus [12, 13]. Caffeine abuse, dietary factors, temporomandibular joint and cervical diseases have also been described as contributing factors [14–16].

Tinnitus is believed to be a central phenomenon that follows an initial peripheral damage [17–19]. The cochlear and/or auditory nerve damage may be permanent, temporary or even subclinical and central neuroplasticity, including decrease of efferent inhibition, tonotopical reorganization and activation of, or modulation by, non-auditory areas have been demonstrated to account for many tinnitus features [17, 18]. Despite the general consensus regarding the role of peripheral damage on the onset of tinnitus, many other factors contribute to tinnitus distress [20]. The correlation of tinnitus improvement and hearing loss recovery in sudden sensorineural hearing loss exists, but is not robust [20]. Nevertheless, peripheral aspects of tinnitus may not be ruled out even in chronic tinnitus, considering that around 45% of the patients submitted to VIII pair neurectomy experimented tinnitus improvement [21]. Ménière disease, particularly, may be an important example of 'peripheral' tinnitus, considering that in the initial stages tinnitus (as well as the other symptoms) is intermittent and acute, with no sufficient time for the arousal of a fully manifested neuroplasticity.

3. Tinnitus characteristics in Ménière disease

According to the criteria of AAO-HNS, MD clue symptoms are recurrent vertigo, fluctuating hearing loss and tinnitus or aural fullness sensation [4, 22]. Tinnitus is probably the less studied of these symptoms, although specific characteristics of MD tinnitus have been observed [23].

First of all, tinnitus is rarely one of the first symptoms noticed (vertigo is the usual one) [23]. Tinnitus is reported by 94% of the patients and considered important by 37% of them [24]. As the years pass and MD disease attacks become more frequent, tinnitus may become permanent and more severe [23, 24].

As tinnitus is usually related to hearing loss, it is not a surprise that MD tinnitus is often low frequencies tinnitus (125/250 Hz) [23]. Nevertheless, according to some studies, this low pitched tinnitus is better tolerated than the high pitched ones [23].

Tinnitus was found to be a less disabling symptom than vertigo by most of the patients [23]. Nevertheless, some patients consider tinnitus an important symptom, and for 19% of MD patients, tinnitus is the most severe complaint, although not associated with a relevant impact in general health and quality of life [24, 25]. According to some studies, the severity of tinnitus does not seem to correlate with the severity of vertigo attacks [23], suggesting that vestibular and cochlear aspects of MD may be independent at some level. On the other hand, some studies demonstrated a strong association between tinnitus and other Ménière symptoms [26].

Diuretics have been proposed as a valuable treatment for Ménière's disease, although the level of evidence concerning their efficacy is low [27]. The eventual side effects of diuretic therapy must not be ruled out as a co-factor for tinnitus development, if we consider its direct ototoxicity and the possibility of excessive decrease of the blood pressure, which, according to some authors, may account for direct perfusion/reperfusion changes in the inner ear [27].

The controversial issue concerning the hypothetical 'cochlear Ménière' is still a challenge. Current AAO-HNS definitions do not allow this possibility [22], but there is some evidence that it might exist [28–30], so it opens a window for the establishment of a tinnitus subtype. According to some authors, MD may begin with cochlear symptoms only, which may be attributed to other diseases related to hearing loss [30]. According to one study, tinnitus is the first symptom in 6.6% of the cases and the median time frame to develop the symptomatic triad in such cases is 3 years [30]. Having said so, it may be possible that cochlear symptoms occur without vertigo, at least for an initial time frame. The Ménière's Disease Index (MDI) was developed as an objective correlation of MD, based on audiometric (pure-tone audiometry air threshold at 125 Hz and pure-tone audiometry air threshold at 8000 Hz) and transtympanic electrocochleography (summation potential amplitude at 4000 Hz) data [28]. A recent study evaluated the MDI scores in patients with audiological symptoms and without vertigo, concluding that the 'cochlear MD' patients may represent a separate clinical entity, with MD's resembling pathophysiology and/or endolymphatic hydrops ('Ménière-like') [29]. A typical case is represented below. **Figure 1** shows the audiometric findings of a possible cochlear Ménière disease with tinnitus. This is a 32-year-old woman with complaints of tinnitus and aural fullness at the right ear. She had no vertigo or



Figure 1. Pure tone audiometry of a 32-year-old woman with left ear tinnitus pitched at 250 Hz and no vertigo or other forms of dizziness/imbalance. Intracanal ECoG showed a high SP/AP ratio (40%) in the left ear. This may represent a cochlear form of MD with tinnitus as the sole complaint.

other forms of dizziness or imbalance. Physical otolaryngological exam was normal. Pure tone audiometry revealed a mild sensorineural hearing loss at the low frequencies on the right ear. Tinnitus pitch matching was centred in 250 Hz. The electrocochleography with ear canal electrode showed a high SP/AP relationship (40%) in the right ear. This may represent a typical case of 'cochlear Ménière' in which tinnitus was the major complaint.

4. Possible treatment implications

Tinnitus treatment is still a challenge. There is no FDA-approved drug for tinnitus treatment and most of the clinical trials with drugs were not replicated, probably due to differences in the samples, tinnitus characteristics, methodology and drug dosage [31]. According to the recent consensus of the AAO-HNS, treatment should focus on counselling, auditory stimulation and cognitive behavioural therapy [11]. On the other hand, according to many researchers there is no reason that tinnitus could not be pharmacologically targeted, considering the multiple neurotransmitters and receptors involved in tinnitus pathophysiology [32]. The

main goal of pharmacological treatment is to deliver the drug, to the right place, in the right amount, in other words, subtyping tinnitus. Understanding the neurochemistry at the peripheral and central areas involved in tinnitus is an important path to follow and may result in the development of successful therapies [31]. Following this line of thinking, if there should be a Ménière's related tinnitus, this could be a possible pharmacological target.

There is a general lack of studies that analyse the effects of MD treatment on tinnitus distress. In a retrospective study comparing patients with vestibular disorders that were treated or not with betahistine 24 mg bid, tinnitus improvement was significantly better in the group treated with betahistine [33]. There was no mention of the type of vestibular disorders included. These findings, although not specific for MD, may encourage further studies, considering that higher doses of betahistine (even reaching 288–480 mg/day) that have been safely employed to MD treatment could also be tried at patients with tinnitus [34].

Recently, it has been demonstrated that nasal oxytocin could induce an immediate decrease in tinnitus volume [35]. Oxytocin and vasopressin receptors are found at the cochlea and were demonstrated to be related to fluid regulation in the inner ear, via inner ear AQPs [6]. Although central effects of oxytocin may also play a role in tinnitus treatment, this immediate effect may be related to some kind of hydrops reduction.

In the last years, cochlear implants have been indicated for alleviating tinnitus, with encouraging results [11]. One study evaluated the effects of cochlear implants in patients with severe sensorineural hearing loss and Ménière's disease. Tinnitus distress, evaluated by the Tinnitus Handicap Inventory (THI) questionnaire, was significantly reduced in patients with MD (14 points decrease 6 months after the implantation, $p = 0.002$) [36].

5. Conclusions

Although, tinnitus is well known as a component of MD spectrum of symptoms, there is some evidence that it may occur alongside with other auditory symptoms in the absence of vertigo or other forms of dizziness. Understanding MD as a possible tinnitus subtype may unveil an important opportunity to study further tinnitus treatment strategies, such as betahistine, oxytocin and cochlear implants.

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